9.09J/7.29J - Cellular Neurobiology, Spring 2005
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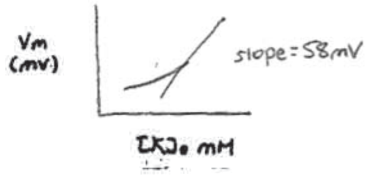
Lecture notes courtesy of Wyan-Ching Mimi Lee. Used with permission.

2/17/04

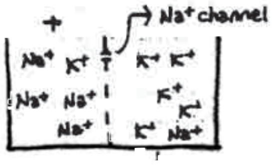
$E_K \sim V_r$ (not exactly, but close enough)

- change molar concentration on outside, see if E_K changes in predictable fashion
  - changing $[K^+]_o$ by factor of 10 changes E_K by 58mV
  - however, at lower values of $[K^+]_o$, something else happens



to determine resting potential, need to take into account E_{Na} as well as E_K

- 99 K^+ holes for each 1 Na^+ hole
  error on terms of ~10%
  (high $[Na^+]$ trying to get through, few channels to go through)



P_{Na} P_{Na}/P_K ← permeability (weights concentrations): measure w/ radioactive K^+ or Na^+, look at rate of diffusion

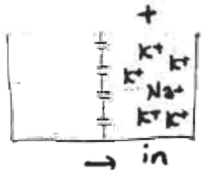
Nernst equation: $$V_m = 58\text{mV} \log \frac{[K^+]_o + [Na^+]_o + P_{Cl}/P_K [Cl^-]_{o;i}}{[K^+]_i + P_{Na}/P_K [Na^+]_i + P_{Cl}/P_K [Cl^-]_{i;o}}$$

becomes Goldman equation (at high negative V_rs, predicts V_r)

$[Na^+]_o$ so much higher than $[K^+]_o$ that adds appreciable current drive at lower $[K^+]_o$

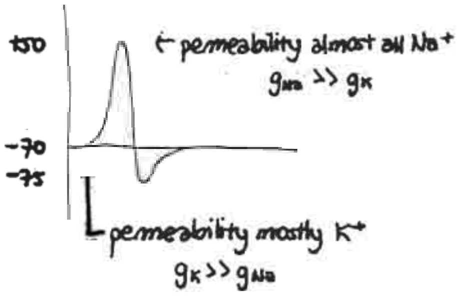
- resting potential from gradients + ion-selective channels + pumps

if Na^+-permeable membrane only



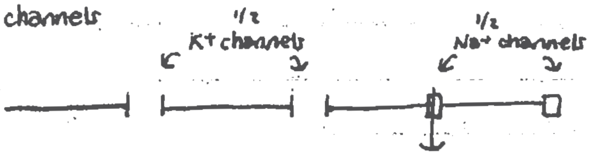
cell would be inside positive
$V = 58\text{mV} \log \frac{[Na]_o}{[Na]_i}$
~58 mV (pos. inside)
similar to top of action potential

- action potential switches membrane conductance to ions

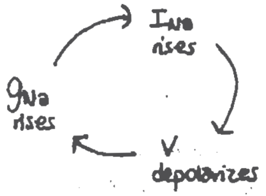


change outside concentration of Na^+: removing ½ Na^+ + replacing w/ impermeant ion decreases maximum of action potential

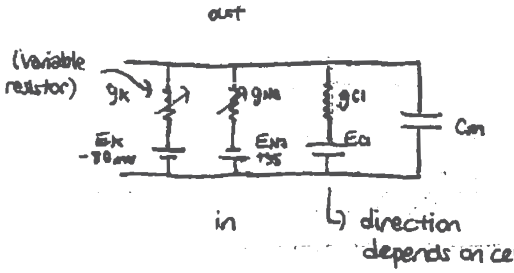
- switching of ion channel conductances based on threshold voltage (-58 mV)
  - these are voltage-gated channels



Na+ w/ depolarization,
depolarizes more,
positive feedback process



positive feedback cycle
(explains threshold)



equivalent circuit for membrane

pumps give you gradients (pumps not batteries)

voltage from gradient is battery

Ohm's Law for membranes - $I = \cancel{VR}\ V/R$

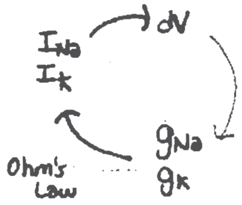
$I = gV$

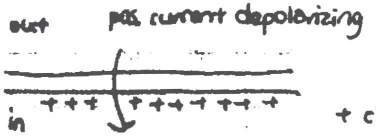
$I = I_K + I_{Na}$

$= g_K (\overset{V_m - E_K}{\cancel{E_K - V_m}}) + g_{Na} (V_m - E_{Na})$ (Ohm's law for individual membrane currents)

inward flow of positive ions → negative current
(textbook uses this convention, Hodgkin/Huxley use other)

when $V_m = 0$, g_K <u>not</u> 0, so must be proportional to where V_m is and where E_K wants it to be





+ charges repelled to membrane

know I, know ~~V~~ ΔV ($\frac{dV}{dt}$)

all current/charges come in to charge, ~~dist~~ discharge C_m

1. mol electrons must be compensated

$Q = CV$ (definition of capacitance)

(voltage across plates × voltage)

$$\frac{dQ}{dt} = \frac{dV}{dt}(C) \times V\frac{dC}{dt}$$

↳ no $\frac{dC}{dt}$

$$I = -C\frac{dV}{dt}$$

all lipid bilayer membranes have ~ same capacitance

$= 1\mu F/cm^2$

$m\Omega \times 1\mu F = 1s$ (for RC time constants)

if you know I and C,

know new voltage

- can reconstruct action potential

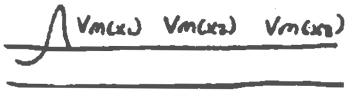
(measure g_{Na}, g_K)

↳ see how g_{Na}, g_K vary w/ voltage

measuring these is holy grail

Hodgkin + Huxley experiments:

- measure g_K, g_{Na}
  - but in unconstrained axon, $V_m(x_1)$, $V_m(x_2)$, $V_m(x_3)$ all different



each patch at different voltage, also influencing each other (current flow between them)

(don't know details)

problems:

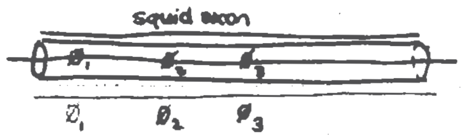
1. spatial variation in V_m
2. temporal variation in V_m
3. how to separate I_K, I_{Na}?

even in individual ~~path,~~ patch, V_m will change (can't measure g as fx of V_m)

will get Na^+ and K^+ currents: how to differentiate? will only get one electrically measured current

1. H + H eliminated spatial variation in V_m by putting wire inside axon, close ones outside: short circuits changes in potential

Space clamp



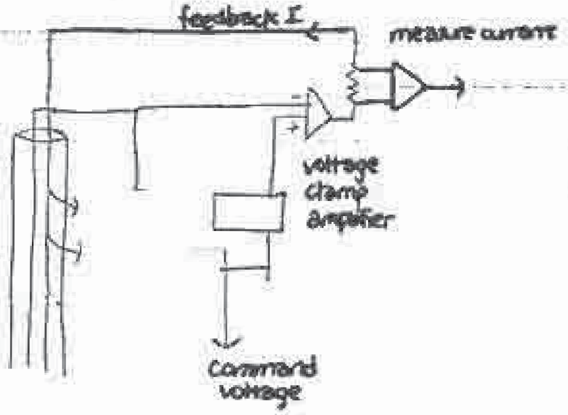
all salt water outside close to membrane will also be at same potential

all inside will be at one potential b/c wire is good conductor, current will flow to eliminate voltage (Ohm's Law w/ hardly any R)

no electric field inside conductor

2. H+H used electronics to artificially clamp Vm where they wanted it

- inject currents In to keep Vm at one value (small values of μAs, nAs)



inject positive current if inside negative

will settle down if no input to amplifier

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